Registered at the G.P.O., Sydney, for Transmission by Post as a Newspaper. Published Weekly.

THE MEDICAL JOURNAL OF AUSTRALIA

(With which "The Australasian Medical Gazette," and "The Australian Medical Journal" are incorporated.)

Journal of the Australian Branches of the British Medical Association.

V[illegible]TH YEAR—No. 7. SYDNEY: SATURDAY, FEBRUARY 17, 1917. PRICE 6D.

MAR 27 1917
MINN. OPHTH. SOC.
LIBRARY

TRADE MARK

The 'Allenburys' Foods

SPECIAL ADVANTAGES

1—The close conformity in composition of the Milk Foods to human milk; both fat and proteids being in similar relative proportions.
2—The readiness with which the Foods are assimilated; being as easy of digestion as maternal milk.
3—Their adaptability as an adjuvant to breast feeding during the period of weaning; no digestive troubles being likely to occur.
4—The freedom from all harmful bacteria; being made from fresh milk, modified, evaporated at a low temperature, in vacuo, and preserved in hermetically sealed tins.
5—The ease and exactness with which the Foods can be prepared; the addition of hot water only being necessary.
6—Fresh elements of diet can be easily added to the Foods, and are specifically mentioned on each tin.

A reliable substitute is thus provided for the Mother's Milk, when this is wanting or deficient.

MILK FOOD No. 1. From birth to 3 months

MILK FOOD No. 2. From 3 to 7 months.

MALTED FOOD No. 3. From 7 months upwards

THE "ALLENBURYS" RUSKS (MALTED).
A valuable addition to baby's dietary when 10 months old and after

A descriptive Pamphlet, giving Analyses, etc., and Samples of the Foods, will be sent on request.

ALLEN & HANBURYS LIMITED
LONDON AND SYDNEY

Made in Australia

by Australians

TRADE **ASPIRIN** MARK

POWDER AND TABLETS

Asserted by Mr. W. M. HUGHES to be Purer than German

Manufactured under license from the Attorney-General of the Commonwealth Government of Australia, and under the supervision of the Federal Commonwealth Analyst, who tests each day's manufacture of SN Brand Aspirin Powder and Tablets before it is offered to the Public.

This guarantees the absolute purity of the SN Brand Aspirin.

Extract from "Herald," Melbourne, Sept. 7th, 1915:—

"A test was carried out on Tuesday by the Federal Commonwealth Analyst, in the presence of the Attorney-General, of Preparations, including those of Bayer and Company, of Germany, and Mr. Geo. R. Nicholas.

"'Of these,' said Mr. Hughes, 'only that prepared by Mr. Geo. R. Nicholas was found to be absolutely pure. In the circumstances, therefore, the Australian Medical Profession has the positive assurance of the absolute purity of the Australian-made drug; that it contains no free Salicylic Acid, and that it in all respects complies with the requirements of the British Pharmacopoeia'."

The Certificates issued by the Federal Commonwealth Analyst, showing the Purity of the SN Aspirin Powder and Tablets, are available for Inspection by any Member of the Medical Profession at the office of the Manufacturers.

The Medical Practitioners are assured that in prescribing Geo. Nicholas SN Brand Aspirin they will be obtaining the highest standard of purity.

The Manufacturers are in the position to supply all demands, and would be grateful to learn whether any difficulty is found in having the SN ASPIRIN dispensed in their prescriptions.

A Free Sample will be posted to any Member of the Medical Profession upon application.

Obtainable through all wholesale Drug Houses.

GEO. R. NICHOLAS & CO.,

SYNTHETIC CHEMISTS,

325 Flinders Lane, Melbourne.

THE MEDICAL JOURNAL OF AUSTRALIA.

VOL. I.—4TH YEAR. SYDNEY: SATURDAY, FEBRUARY 17, 1917. No. 7.

A CLINICAL AND ANATOMICAL REPORT OF A CASE OF FRIEDREICH'S DISEASE.[1]

By **W. F. Litchfield, M.B. (Syd.),**

Honorary Assistant Physician, Royal Alexandra Hospital for Children, Honorary Assistant Pathologist, Royal Prince Alfred Hospital, Sydney;

Oliver Latham, M.B., M.Ch. (Syd.),

Pathologist to the Lunacy Department, New South Wales;

and

A. W. Campbell, M.D., C.M. (Edin.),

Sydney.

Blanks in our knowledge of Friedreich's disease, in particular of its ætiology and pathology, necessitate the investigation of more cases; accordingly we feel it a duty to publish this report.

For the clinical observations one of us (W.F.L.) is responsible; another (O.L.) has undertaken the pathological examination.

Clinical Report by Dr. W. F. Litchfield.

M.F., a girl, aged eight years, was admitted to the Royal Alexandra Hospital for Children on July 6, 1916. She was said to be suffering from Friedreich's ataxia, and it was reported that a brother, aged 14 years, had recently died of that disease, and that another brother, aged five years, had similar symptoms. The parents noticed that the patient walked in "a wabbling fashion" two years before, and since then had been getting thinner and weaker, and was liable to fall over in the dark. More recently she had gone off her feet, and at the time of admission could not walk or sit up without support. Since her illness began she had become nervous and emotional. The parents did not notice any alteration in her speech. The parents are healthy, and live in the country. There is no history of a similar affection in the antecedents or collateral relations. Nine children were born to the parents:

W.F., a boy, 14 years, died in May, 1916, of Friedreich's ataxia.

E.F., a girl, 12 years, now convalescing from typhoid fever.

E.F., a boy, 10 years, "a nervous boy."

M.F., a girl, 8 years, the patient.

S.F., a girl, 6 years, has twitching of the face.

C.F., a boy, 5 years, has ataxia.

C.F., a boy, 4 years, healthy.

A.F., a boy, 3 years, healthy.

Baby, ?, 7 months, healthy.

When examined, the patient lay quietly and placidly in bed, but when approached she cried in an irritable and emotional manner and was loath to comply with requests. In the light of her subsequent history, part of her weakness was no doubt due to an oncoming typhoid fever. With patience, however, it was ascertained that she had a very distinct ataxia, with some jerkiness in the movements of the hands. The gait could not be tested, owing to her weakness. The speech did not seem to be affected. There was an inconstant nystagmus on lateral deviations of the eyes. There was *pes cavus* on each side, but no curvature of the spine. The knee-jerk was absent and the plantar reflex was feeble, but flexor in type. There was some loss of tone of the muscles, but no loss of sensation could be made out.

One week after admission an irregular fever developed, which ultimately became typhoid in character, and death occurred on July 26, 1916.

A post-mortem examination was held. The Peyer's patches and the solitary follicles of the ileum and colon were found enlarged, as well as the spleen and many mesenteric glands. The spinal cord and brain were removed in one piece and sent to Dr. O. Latham at the Medical School, where they were subsequently examined in detail by him, in conjunction with Dr. A. W. Campbell, who also saw the child with me before death. They will record their findings separately.

The history of the boy who died, as far as could be gleaned from the parents and Dr. H. Lister, who saw him twice at intervals, and who kindly sent some notes, was as follows: His symptoms began at the age of six years. He had ataxia of the arms and legs, and later nystagmus. There was also mental irritability and some affection of the speech. He died in May, 1916, of typhoid fever, at the age of 14 years.

The other boy, C.F., aged 5 years, was admitted to the hospital on July 25, 1916. His symptoms were said to be of three months' duration. On examination, he was found to have a swaying ataxia on standing and walking. There was also slight but distinct ataxia of the hands. *Pes cavus* was present in a slight form. The knee-jerks could not be obtained; the speech was normal, and there were no sensory disturbances or nystagmus. The muscles were somewhat slack, and he was shy and uncertain in his temper. About two weeks after admission he contracted typhoid fever. He recovered, and was allowed out of bed five weeks later. After convalescence he was much improved, it being difficult to detect any ataxia of the arms or legs. He ran about the ward in quite a normal way. He went home a few days ago. As the rest in bed seemed to improve his condition, I advised his father to practise rest as a form of treatment, and, as a working method, to keep him in bed on alternate days. This would mean that he would rest for one hundred and eighty-seven days in the year, and it would be less irksome than staying in bed for several days at intervals.

If, following Gowers, we regard the disease as an inherent and congenital lack of vitality of certain functionating nerve tracts, it is reasonable to sup-

[1] Communicated to the New South Wales Branch of the British Medical Association at a Meeting held on November 24, 1916.

pose that stress of function would hasten the degeneration of the tracts and rest retard, if not arrest, the process.

Pathological Report by Dr. Oliver Latham.

The brain and spinal cord from Dr. Litchfield's patient were examined at the Pathological Laboratory of the Lunacy Department of the New South Wales Government.

A. *Macroscopical.*—The material was received in 10% formalin, and on naked eye examination the brain appeared normal, the halves of both cerebrum and cerebellum being equal in size and general form. The cord, on the other hand, seemed small, even for a child of 8 years, especially in the dorsal region. At the level of the fifth lumbar segment the lateral measurement was 8.8 mm. and the dorso-ventral was 6.5 mm. The measurements of the lower dorsal segments were 8.9 m.m. × 6.0 mm. and 8.8 mm. × 4.8 mm., and those of the lower cervical regions 10.8 mm. × 6.2 mm. and 11.5 mm. × 7.0 mm. The lateral measurements of the cord at the level of the first cervical segment, just below the crossing of the pyramids, were 16% less than those of a normal cord of an adult at the same level, and the dorso-ventral measurements were 33% less. The cord at this situation was therefore 23% smaller than a normal cord of an adult. Even if allowance be made for the fact that the cord was a little flattened, it was to be expected that the other differences in measurement would be proportional. This proved to be the case, except in regard to the length of the posterior septum, which was but half as long. There was, therefore, a relative diminution in the area of the posterior columns, and an increase in the ratio of grey matter to white, in contradistinction to what Llewellys F. Barker[7] found in his cases.

B. *Microscopical.*—The following methods were employed: (*i.*) Weigert's and Heller's methods used for tissues mordanted according to Weigert's formula, (*ii.*) Marchi's or Busch's staining for degenerating myelin, (*iii.*) Nissl's method for nerve cells and round cell infiltration, (*iv.*) van Gieson's stain on Heller's preparations for neuroglia, and (*v.*) hæmatoxylin and eosin for vascular and interstitial tissues.

I.—Spinal Cord.

Examination of sections of the cord at different levels:—

Second Sacral (Fig. I.)—A comparison of the posterior columns with the rest of the section reveals a marked diminution of the myelin fibres. The root zones and the posterior ventral fields have escaped to some extent. The lateral columns are pale in the position of the lateral pyramidal tracts. The anterior nerve roots are quite normal, while the posterior nerve roots show distinct but not excessive loss of myelinated fibres. The fine fibres of the grey matter also appear normal. The anterior cornual cells stain well by Nissl's method. The central canal is primitive in structure, being represented by a vertical slit lined by a regular row of cells, in places but one cell deep. The pia-arachnoid is not thickened nor infiltrated with cells at this or any other level, save about the fifth dorsal segment, where a slight thickening occurs over the posterior columns. The blood-vessels are normal, neither hyaline degeneration, endarteritis nor perivascular infiltration being detectable.

Fifth Lumbar (Fig. II.)—The changes seen in the second sacral segment are seen in this section; the sclerosis in the posterior columns, however, is much more marked. Except for the ventral fields and root zones, the posterior columns are entirely occupied by a peculiar sclerosis, having the appearance of bands or whorls of interlacing fibrils, somewhat similar to those met with in disseminated sclerosis and neurofibromatosis. Here and there a few normal myelinated fibres are to be seen. Flechsig's oval field has apparently escaped. There is a distinct pallor in the postero-lateral columns, and a little on either side of the antero-median fissure. "Busch preparations" at this level reveal but few degenerated myelin fibres in the posterior columns, where the sclerosis is very extensive. Many scattered degenerating fibres, however, may be seen round the margin of the cord, extending in more deeply just external to the posterior horn. In sections stained by Nissl's method the cells in the grey matter stain in a perfectly normal manner. It is noteworthy that the peculiar glial phenomena are only present in the oldest parts of the lesions.

Second Lumbar (Fig. III.)—The sclerosis is still more marked at this level. The entering root zones and the posterior ventral zones are preserved to a great extent; this obtains throughout the cord. Flechsig's oval field is to some extent evident. The central canal is transverse. "Busch preparations" are similar to those described in the preceding paragraph, but the conditions noted in the dorsal regions in sections prepared in this way can be detected in them. In other respects the histological appearances are similar to those met with in the sacral and lumbar cord.

Seventh and Eighth Dorsal (Fig. IV.)—At this level it is seen that the area corresponding to Goll's columns is distinctly more affected than Burdach's columns; a few fibres persist in the situation corresponding to Hoche's bundle higher up in the cord. There is distinct pallor in the crossed pyramidal and direct cerebellar tracts; this is due to a diminution of fibres and to the presence of old-standing sclerosis.

Sections at this level prepared according to Busch's and Marchi's methods (Fig. XII.) show scarcely any degenerated myelin fibres in the posterior columns, where the sclerosis is almost complete. In the regions occupied by the crossed pyramidal tracts the direct cerebellar tracts and the antero-lateral tracts of Gowers, and in part in those occupied by the direct pyramidal tracts there is a very obvious degeneration. The lesion is, however, by no means extensive. The fibres can be counted. It cannot be said that the degenerated fibres occupy the exact position of the tracts mentioned. In no part can this acute degeneration be described as a mass degeneration. There is more degeneration in the position of the direct cerebellar and crossed pyramidal tracts than elsewhere, and in other situations

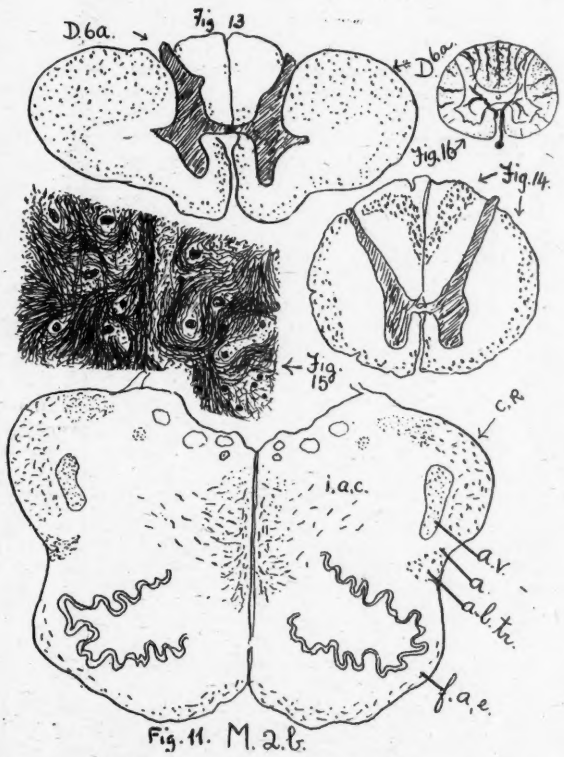
there is more in the marginal than in the central regions. There does not appear to be any special collection of affected fibres in the antero-lateral tract of Gowers. The foregoing points may be verified by inspecting Figure XII. with a hand lens, each black dot representing a diseased fibre.

Clarke's columns show up well in the sections stained by Nissl's method, no less than 12 cells on one side and 9 on the other being present. After a careful examination of sections at many levels from the second dorsal to the tenth dorsal, it was determined that there was a diminution in the number of cells of normal size and staining properties; many of the cells appeared to be shrunken.

Fifth Dorsal (Fig. V.)—At this level an almost complete sclerosis of Goll's column, and a partial sclerosis of Burdach's column is noted, while the root zones and the posterior ventral fields are fairly well preserved.

Fifth and Fourth Cervical (Figs. VI. and VII.) — The intensely sclerosed central area forms a V-shaped figure, whose angle or point approaches nearer the grey commisure in the fifth cervical segment than in the fourth. The central canal is vertical in the fourth cervical segment, and is more complicated in structure than at the lower levels. Sections stained by Marchi's method reveal changes similar to those described above. The anterior cornual nerve-cells appear normal in the sections stained by Nissl's method.

First Cervical. — A moderately extensive sclerosis extends deeply into the region of the crossed pyramidal tracts and a little into the direct pyramidal tracts as well.



Figs. XI., XIII., XIV. and XV. (For descriptions see page 139.)

II.—Medulla and Pons.

At the crossing of the pyramids (Fig. VIII.) the *nuclei graciles* and Goll's columns are most affected. A section of the medulla (Fig. IX.) about the middle of the olive reveals distinct pallor of the restiform body and of the regions around the *nuclei graciles* and *cuneati*; this also affects the external arciform fibres and mesial fillet. Sections of these regions stained by Nissl's method show that the nerve-cells are quite normal. Special attention has been paid to the olives and to the various nuclei. The red nuclei are also normal in appearance.

A Marchi preparation of the medulla about the middle of the olives (Figs. X. and XI.) shows degenerated fibres in the *lemniscus* or mesial fillet, a few in the region of the external arciform fibres, a few anterior to and near the *nuclei graciles* and *cuneati* (internal arcuate fibres) and a considerable number in the restiform body and in a field which seems to be the root of the fifth cranial nerve, and which lies to the ventral and internal side of the commencement of the restiform body and antero-lateral tracts.

III.—Cerebellum.

No abnormality has been detected in sections prepared by Nissl's method of the cortex and dentate nuclei.

IV.—Posterior Spinal Ganglion.

Only one of the posterior spinal ganglia was recovered. This came from the mid-dorsal region. It was studied carefully after staining by Nissl's method and with hæmatoxylin and van Gieson's stain. It was not quite healthy, but the number of degenerated cells seen was few. There were no interstitial changes, and practically no disappearance of cells.

V.—Cortex Cerebri.

Many sections of the cortex, especially from the precentral and postcentral gyri, were examined. The former appeared to be normal, but in the postcentral gyrus, toward the floor of the fissure of Rolando degenerative changes similar to those met with in *tabes dorsalis* were seen. The changes affect the large pyramidal cells chiefly; many of these cells are shrunken and devoid of processes, but the lamination generally is disordered. No vascular or glial changes were noted.

VI.—Other Parts.

Some "Busch preparations" were made (*a*) through the posterior part of the internal capsule and (*b*) in the region including the radiating fibres to the area of Rolando. Some acutely degenerated fibres were found scattered throughout these sections. These fibres probably belong to the cerebral portion of the sensory tract.

VII.—Commentary.

From the foregoing it will be seen that we are dealing with a relatively old sclerosis affecting parts of the posterior tracts, in which the interstitial tissue has assumed an unusual type, resembling

that found in disseminated sclerosis. An irregular but less marked sclerosis, of considerable duration, is also present in the lateral regions of the cord. This sclerosis involves areas which do not correspond to sharply defined tracts, and is associated with a much more recent degeneration, revealed by Marchi's method of staining. These changes can be traced beyond the medulla, and there are faint indications of them in the cerebrum. At the same time we do not find any marked changes in the pia-arachnoid, blood-vessels or lymphatic glands of the cord or brain. Moreover, we have noted a normal condition of the nerve cells, save a few in Clarke's column and the large cells in the postcentral gyrus, as well as a few in the posterior spinal ganglia.

While the changes described have much in common with the pathological findings commonly noted in Friedreich's hereditary ataxia, there are some important differences. The lateral columns are not severely sclerosed, but since early changes are seen in these columns in the sections stained by Marchi's method, it is possible that, had the patient lived longer, a more typical picture would have developed. In the next place there is no gross atrophy of the cerebellum, and the dentate nuclei, the olives and red nuclei are quite normal. The changes described bear a certain pathological resemblance to Gower's ataxic paraplegia, especially in the escape of the posterior root zones and ventral fields.

Some observers have called attention to the fact that many of the lesions described above are situated in the areas supplied by the posterior arterial system, *i.e.*, by a number of small blood-vessels derived from the pia-arachnoid. They suggest that a toxin exists in the blood and can exert its action on the tissues most readily in these situations. In this connexion it may be well to recall certain toxic conditions which at times give rise to lesions of a somewhat similar nature in the spinal cord. I refer to pellagra, pernicious anæmia, diabetes and toxic conditions associated with infection. On reviewing the histological findings in this case in the light of this theory, I would wish to make reference to some experimental work conducted by Orr and Rows.[1] These observers inserted celloidin capsules containing bacteria in the immediate neighbourhood of large nerves, such as the sciatic nerve. The results produced in this manner in nerves, posterior spinal ganglia, nerve roots, pia-arachnoid, myelinated fibres, including definite tracts, neuroglia, nerve cells and the adventitia of blood-vessels resembled in a remarkable manner the pathological changes found in *tabes dorsalis*. They called the condition induced "lymphogenous intoxication." It included both inflammatory and proliferative phenomena.

More recently the same observers have induced a diffuse plastic inflammation of the peritoneum by laying celloidin capsules containing bacteria by the side of the stomach, kidneys or coils of intestines. In these cases they found somewhat similar changes in the sympathetic nerves and ganglia, while degenerative rather than proliferative changes were produced in the posterior spinal ganglia and cord, the nerve cells escaping. They held that the spinal ganglia and cord had been acted upon by a "hæmatogenous intoxication." They noted that those areas supplied by the anterior spinal artery escaped to a large extent, while the peripheral parts of the cord, supplied by the pial arteries bore the brunt of the changes. They likened this distribution to that observed in cancer of the peritoneum, Addison's disease, pernicious anæmia, pellagra, etc. It was thought, however, that the changes observed could not be ascribed exclusively to hæmatogenous causes. On the other hand, they could not be explained solely as a result of lesions in the sympathetic system, which was involved in the experiments. It is reasonable to assume that lesions of the sympathetic system might effect an alteration in the action of some of the ductless glands. They, therefore, suggested a combined influence.

In presenting this account of the pathological changes in a case of Friedreich's disease, I would draw attention to the occasional hereditary and familial nature of the disease, and also to the undoubted peculiar nature of the neuroglia which takes the place of the degenerated myelin fibres, in a manner analogous to that seen in the neuroglial reaction in disseminated sclerosis, neurofibromatosis, gliomatosis and syringomyelia. These are conditions whose ætiology many observers tend to connect with developmental defects, although a developmental origin is not actually proven, at all events as far as disseminated sclerosis is concerned.[2] In a case which I described in *The Medical Journal of Australia*[3] lesions at several levels were noted which were as likely to be the results of toxic as of developmental causes.

May I suggest that more than one of these factors may also prove to be at work in conditions hitherto grouped as forming the entity Friedreich's ataxia, and that the different pictures occurring in different cases may depend on a relative predominance of one or other factor in the ætiology?

DESCRIPTION OF PLATES.

PLATE I.

Fig. I.—A rather thick "Heller" section. Pallor on either side of the postero-median septum. The anterior spinal nerves are quite healthy.

Fig. II.—The sclerosis in the posterior columns has become more marked.

Fig. III.—O = Flechsig's oval field; this tends to escape, as also do the postero-ventral fields and the posterior root zones.

Fig. IV.—H. O. Hoche's bundles, which partially escape. The sclerosis is here at its height.

Fig. V.—This section shows the pia-arachnoid, slightly thickened over the posterior columns. The posterior nerve roots stain fairly well, though not as well as the anterior. A moderate degree of pallor in the crossed pyramidal, Gower's and more anterior areas of the cord can be discerned.

Fig. VI.—The chief sclerosis is now confined to what approximately corresponds to Goll's columns.

Remarks by Dr. A. W. Campbell.

Since I have had the double advantage of seeing the subject of these notes while she was under Dr. Litchfield's care and of studying the beautiful series of microscopic specimens prepared by Dr. Latham, I have acceded to a request to contribute these remarks.

Taking first the pathological changes, as Dr.

PLATES ILLUSTRATING DR. OLIVER LATHAM'S ARTICLE.

PLATE I.

Fig. I.

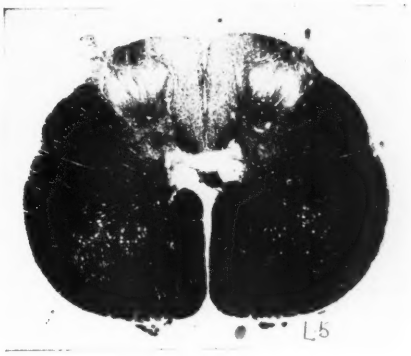


Fig. II.

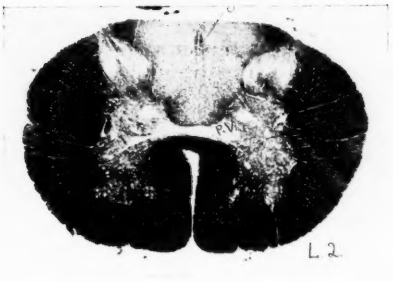


Fig. III.

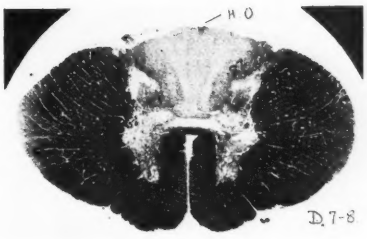


Fig. IV.

Fig. V.

Fig. VI.

PLATES ILLUSTRATING DR. OLIVER LATHAM'S ARTICLE.

PLATE II.

Fig. VII.

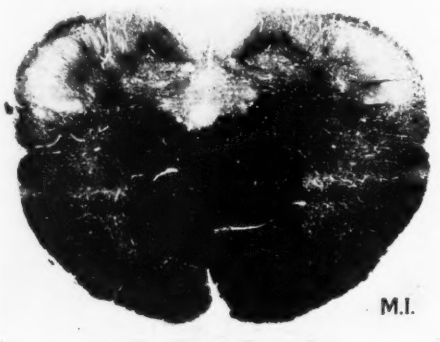


Fig. VIII.

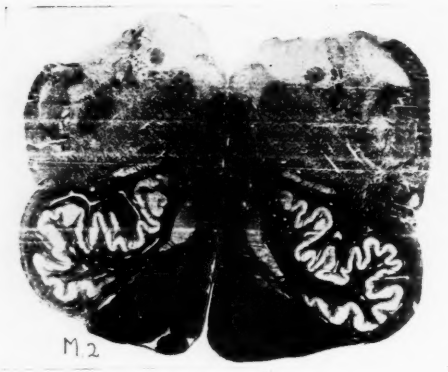


Fig. IX.

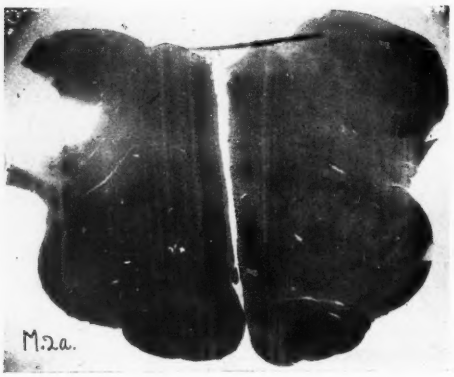


Fig. X.

Fig. XII.

Latham has shown, in this cord there are two morbid processes, one old-standing, the other acute. By the old-standing process—a process which must have been in existence at least one year and possibly several years—the posterior columns from the lower lumbar region upwards are swept bare of healthy fibres, with the exception of the posterior root zone and the cornu-commissural zone, and even these cannot be said to be quite healthy. Also as a result of the old-standing process, the dorso-lateral columns in the position of the direct cerebellar and the crossed pyramidal tracts are partially sclerosed.

Regarding the acute process, the method of Marchi reveals diseased fibres practically throughout the lateral and anterior columns—not in the posterior columns, because these, as has been mentioned, are already denuded of fibres. This acute degeneration is not a mass degeneration, the field is merely dotted with countable diseased fibres, which are specially noticeable in the direct cerebellar and crossed pyramidal tracts and along the lateral and anterior margin of the cord. This acute degeneration is difficult to explain; it is not systemic, it might be a "succession degeneration," that is, a degeneration of internuncial and endogenous fibres consequent upon the primary sclerosis; or it might be the product of the typhoid toxæmia which caused the patient's death; or it might be due to an intrinsic toxin.

These then are the chief anatomical findings, and it will be at once noticed that the picture differs from that in most other recorded cases, inasmuch as the dominant and most intense sclerosis does not step over to the lateral columns, but remains confined to the posterior columns. And here it may be added that in this respect the case resembles one recorded in 1899 by Dr. Rennie, of Sydney.[4]

Other changes which are secondary, and certain findings which are negative, and yet important for comparative purposes, will be found in Dr. Latham's report.

Next concerning two symptomatological paradoxes. It is remarkable that in Friedreich's disease we get destruction of posterior columns without the expected degree of disturbance of sensation, and destruction of lateral pyramidal tracts (in most cases) without the expected paralysis. How are we to explain these paradoxes?

First, as to posterior column sclerosis without anæsthesia. In point of fact it is wrong to suppose that in Friedreich's disease sensation is unaffected. It has been shown by Saunders,[5] who examined 20 cases, that if sensibility be properly tested, disorder will invariably be found. (Children are extremely difficult to test, hence our case gave no information on this point.) The facts are that while sensibility to touch, to pain and to heat and cold may be preserved or but little affected, the sense of passive movement and of posture, what is known as deep sensibility, will always be grossly disturbed. Physiologically this is in accordance with what we know of the spinal traject of common sensation. We know that only those fibres which convey impressions of movement and posture ascend in the posterior columns. Fibres for other impressions ascend elsewhere. And the reason why in Friedreich's disease the defect of sensation shows specific characters, and characters different from those found in *tabes dorsalis*, is that in Friedreich's disease there is, as a rule, relatively little affection of the posterior roots and the posterior root zones. In *tabes dorsalis*, on the contrary, disease of the posterior roots is the primary and essential change. In other words, in Friedreich's disease the changes begin intraspinally, in tabes extraspinally

Next, concerning the paradox of lateral pyramidal sclerosis without paralysis. In all the specimens I have examined the sclerosis has not been spread over the whole tract, it has involved only that part in contact with the direct cerebellar tract, the inner part has escaped, and the escape of this inner part, plus the intact direct pyramidal tracts, must account for the absence of paralysis.

Finally, as to the origin of the morbid process, several explanations have been offered. We have the view promulgated by Gowers that there is an inherent tendency to early decay—an abiotrophy—of the parts involved. We have Newton Pitt's view that "there is an inherited tendency to general early vascular degeneration." We have the view favoured in Germany that the primary change is an agenesia, a faulty development of the posterior columns, and that the changes in the lateral columns are secondary or compensatory, thus, the posterior columns being thrown out of action, the lateral tracts attempt vicariously to assume their function and finding themselves overloaded soon degenerate. And lastly, we have Williamson's view[6] that the parts degenerate because they happen to lie in that segment of the cord wherein the blood supply is weak, namely, in the field supplied by the posterior spinal system of arteries.

Of these views I would give my support to that of Williamson, and for the following reasons: To

DESCRIPTION OF PLATES.

PLATE II.

Fig. VII.—Similar to the last. It is interesting to note broadly three degrees of staining, *viz.*, a white central area where the sclerosis is complete, one just outside—grey—showing a more moderate state, and the posterior root zones and ventral fields almost black.

Fig. VIII.—Medulla at crossing of pyramids, showing marked sclerosis of Goll's columns with but moderate involvement of Burdach's.

Fig. IX.—The medulla about the middle of the olive. There is some paling when comparing this section with a normal one, especially in the restiform bodies, and posterior pyramidal decussation, etc.

Figs. X. and XI.—Section of medulla about same level as Fig. IX., stained by Busch's modification of Marchi's method; the affected parts may be the easier made out by referring to a drawing of it in Fig. XI. c.r. = corpus restiforme. a.V. = ascending root of the fifth nerve. a. = external arciform fibres going towards the restiform body. a.l.tr. = Gower's antero-lateral tract. f.a.e. = external arciform fibres. i.a.c. = internal arcuate fibres.

Figs. XII. and XIII.—A Busch preparation from the sixth dorsal segment. The degenerated fibres may best be made out by referring to Fig. XIII., in which many degenerated fibres are seen in the direct cerebellar tracts, and in the crossed pyramidal, antero-lateral of Gower's, and marginally right round and including either side of the antero-median fissure. The posterior columns are too sclerosed to contain many fibres to degenerate.

Fig. XIV.—After Orr & Rows, illustrating "hæmatogenous" infection or intoxication (Marchi's method). It has several points in common with Fig. XII. (Marchi's method), remembering, of course, the whole process in Fig. XIV. is more acute.

Fig. XV.—A *camera lucida* drawing from Fig. IV., to show the whorls of neuroglia proliferation surrounding small blood-vessels, and containing a few undegenerated myelinated fibres on either side of the postero-median septum. Abbé's *camera lucida*, Zeiss AA lens, compensating eyepiece 12, equals a magnification of 180.

Fig. XVI.—Showing parts of the cord supplied (*a*) by anterior spinal artery and (b) small arteries from the pia-arachnoid.

begin with, the degeneration is not a systemic one, and especially not a systemic degeneration of the spino-cerebellar tracts, as many writers assert. The change in the posterior columns seems to be the only change which is present in every case, which is constant and, I think, fundamental. But neither are the posterior columns spino-cerebellar, nor is the degeneration in them systemic, since essential parts, the posterior roots and the posterior root zones, usually escape affection. Again, although we may have an affection of the direct cerebellar tract, other cerebellar tracts, namely, the antero-lateral ascending tract of Gowers, and the rubro-spinal and the vestibulo-spinal tracts are not involved. Further, thrown into the medley we have an affection of a part, and a part only, of the crossed pyramidal tract. Therefore, we have portions of no less than three diverse systems, a sensory tract in the posterior columns (I say nothing of descending tracts in these columns), a cerebellar tract and a motor tract whose degeneration we have to explain. I cannot agree that either abiotrophy or agenesis meets the position.

Furthermore, as Williamson has indicated, the essential changes of Friedreich's disease lie within the area supplied by the posterior system of spinal arteries, and it is remarkable that the same applies to a series of diseases, in which we have reasons for believing that the affection is of hæmatogenous as opposed to lymphogenous origin. These diseases are anæmia with spinal symptoms, "combined sclerosis," spinal syphilis (in certain cases), advanced pellagra and senile paraplegic ataxia. It is not supposed that in these conditions the degeneration is necessarily due to disease of the posterior spinal blood-vessels; the essential point is that there is a sluggishness of circulation within them, whereby nocuous substances when they happen to be present in the blood remain unduly long in contact with the tissues, and so induce degeneration. If the spinal cord in adult life be subject to grave changes of hæmatogenous nature I see no reason why it should not be so in childhood.

It may be urged to the contrary that Friedreich's disease is hereditary. The reply to this is that, while the disease runs in families, it is rarely seen in parent and offspring. The thought arises that the mother must be responsible. It seems rational to suppose that a mother lactating after certain of her pregnancies—possibly after all—may harbour and pass on to her child or children some unknown endotoxin, some noxa, which may gain the infant's blood-stream from the intestinal tract and be specifically prejudicial; that is, lead to the lodgement of toxins in the indicated vulnerable parts of the spinal cord, and to subsequent decay.

References.

[1] Orr and Rows, "Observations on Influence of Toxins," *Journ. of Ment. Sci.*, April, 1914.

[2] Dawson, "The Histology of Disseminated Sclerosis," *Trans. Roy. Soc., Edin.*, Vol. I., Part III., 1916.

[3] *The Medical Journal of Australia*, November, 1914.

[4] Rennie, *Brit. Med. Journ.*, 1899.

[5] Saunders, "Sensory Changes in Friedreich's Disease," *Brain*, 1913.

[6] Williamson, "Diseases of the Spinal Cord," 1908.

[7] Barker, "Anatomical Report of Two Cases of Hereditary Ataxia," *Dec. Pubs.*, Univ. of Chicago, 1903.

Reports of Cases.

CIRRHOSIS OF HÆMOCHROMATOSIS OR BRONZED DIABETES.

By J. C. Verco, M.D.,

Consulting Physician, Adelaide Hospital.

A.B., male, aged 34, was first seen on September 13, 1916. The following history was elicited. He did clerical work until two and a half years ago, when he began storekeeping. From a lad he had been liable to sick headaches, which compelled him to leave his office and go to bed. During the last two or three years these had not been so troublesome. Four and a half years ago he married, without issue. Two years later he took a store, because he would often fall asleep over his clerical work, and thought moving about in the open air would cure this. About the same time his wife noticed his skin getting darker, especially about the loins. Occasionally, too, he would feel a sudden faintness or giddiness, and had to support himself with something for a few seconds; but he regarded this as trivial, and joked about it.

In December, 1915, he took a holiday at the seaside, and, while bathing, his friends saw the sooty tint of his skin, and suggested he might wash himself oftener than once a year. Walking up the ramp at the Adelaide Railway Station a day or two later he suddenly got very faint, and had to stand still for some time, because his heart seemed so bad, and then to take a cab to his lodgings. Fancying this attack was due to the extreme summer heat in the city, he returned at once to Broken Hill and consulted a doctor. He had a cough for a week, and after a coughing fit his heart would seem to stop and then throb and beat so hard in his chest and neck as to be visible to others, and would make him feel quite faint and giddy. Until December he had regarded himself as quite well. He had only spent half a day in bed since an attack of enteric fever, sixteen years before. He had been able to do laborious work without difficulty, and was a champion lacrosse player, and represented New South Wales in Inter-State tournaments. But from the date of the heart-turn in Adelaide he had done no work, except occasionally driving round to collect accounts. The doctor saw him doing this one day, and put him to bed for three weeks, because he appeared to be working, and because he had some giddiness. After several months' treatment he was advised a change; so he went on a farm for more than two months during July, August and September. When he returned home the doctor said the holiday had benefited him, but he would not permit him to go back to work, and told him he had Addison's disease.

He had not taken any alcohol during 1916, and very rarely before. On a very hot day he might have a glass of "shandy," but never more than one. He seldom drank on invitation, drank no alcohol throughout the winter, and had never been intoxicated. He had never had syphilis.

When seen by me on September 13, 1916, his appetite was good and bowels regular; he had not been troubled with piles. His micturition was normal, and he had not to rise at night. He "felt splendid," had no faintness or giddiness, and slept well. He had gained eighteen pounds in weight, and scaled 157½ lbs. There was no ataxy with shut eyes on either foot; his reflexes were normal. His pulse-rate was 84, with about four or six intermissions to the minute, with a blood pressure in the brachial of 144 mm. of Hg. The heart's impulse was obscure; the sounds were natural, but weak. The liver dulness began at the fifth space in the right vertical nipple line; its margin extended to 3½ inches below the costal arch and seven inches from the xiphoid cartilage in the middle line; its surface was smooth, convex in the epigastrium, firm and not tender. The spleen descended during inspiration 1 to 1½ inches below the left costal arch, and was somewhat enlarged upwards; its edge was firm. The abdomen was otherwise normal. The urine was dark and clear. The reaction was acid, and the specific gravity 1.028. There was no albumin nor sugar.

Melasma was very noticeable. The skin of his face, neck, hands and forearms was very dark. Across his loins were sooty, dirty-looking, transverse patches, extending from the sacrum and gradually fading up the back. It was also dark near the angles and bases of the scapulæ, in and near the axillæ, down the inner aspect of the arms, over the lateral region of the chest and flanks, fading out forwards over the front of the thorax. From the ensiform cartilage to the *symphysis pubis* was a conspicuous dark line two millimetres in breadth, a black *linea alba*. The depression of the navel was very dark. The bends of the elbows in front, and of the knees behind were dark, and here was a transverse band, as though he had worn garters (but he had not). The band was at the bottom of the crease in his skin formed by the full flexion of the joint. The melasma did not consist of black dots or spots in a white skin, but of dark, curved, rather broad lines around minute white areas. Neither conjunctivæ, tongue nor the inside of the mouth showed black patches. His hair was thick and black, but he had never had any hair on his face, nor in his armpits, and but little on his pubes. Only a very fine down, which could scarcely be pinched up by the fingernails, existed on his back. He had not taken any arsenic or any other medicine before December, 1915, when his melasma was quite plain to the laity.

His father died of heart disease; his mother was alive, aged 74; he had one brother, aged 27, and four sisters, from 41 to 32, with no family history of diabetes.

An examination of his blood was made at the Government Laboratory, the report read: "Hæmoglobin, 75%; red blood cells, 3,552,000 per c.mm.; colour index, 1.0; white blood cells, 6.100. The red cells show slight aniso-cytosis and slight poikilocytosis. The blood picture is indefinite; it may be that of pernicious anæmia during a remission."

On September 21 he felt well, with no tired feeling, had eaten and slept well, and weighed 159 pounds. The specific gravity of his urine was 1,023, and it contained neither albumin nor sugar. To test his tolerance of sugar, he ate, on September 23, quite three-quarters of a pound of lollies, plenty of jam and cake, and took a lot of sugar in his tea; but his urine passed on the next morning in my room was 1,016, dark, clear, and sugar-free.

On September 28, in the morning, he had a bad turn. Everything about his heart seemed to stop, and then it began to gallop, but only for a few seconds. This recurred at intervals all day, but had disappeared by the next morning. The three previous nights he had had to rise about 2.30 a.m. to pass water. He was eating and sleeping well, and had gained two pounds in weight. He was given *Tr. digitalis*, 0.3; *Liq. arsenicalis*, 0.2; *Tr. cascarillae*, 2.0; *Syr. aromat*, ad 4.0; *ter in die*; also *Tabloid ferrug.* (Blaud), 0.324, *ter in die*, and bone marrow, one teaspoonful, *ter in die*. His urine was sugar-free.

On October 12 his *liquor arsenicalis* was increased to 0.25. His liver and spleen were unchanged, and the urine was sugar-free.

On October 13 the laboratory report read: "Hæmoglobin, 81%; red blood cells, 4,614,000; colour index 0.88; no abnormality in the corpuscles on the film."

On October 26 he felt very well, and was eating and sleeping well. He had no pains and no shortness of breath. He was walking daily as far as he liked. The pulse gave about two big kicks in a minute, and one intermission. The urine continued to be sugar-free. His weight was 160½ lbs.

November 2.—He did not sleep well during two or three nights in the week, and had slight perspirations. His weight had fallen to 159 lbs. The pulse was regular. The urine was high-coloured, 1,030, acid, no albumin, but contained 2.4% of glucose, and a little bile, giving the green tint with *Tr. iodi*.

From this date onwards sugar was never absent, and gradually increased, while his weight as steadily declined.

November 4.—Urine, 36 oz.; sugar, 2.4 % = 3 vii.

November 7.—Urine, 36 oz.; sugar, 2.2 % = 3 vi.

November 8.—Urine, 51 oz.; sugar, 3.2 % = 3 xvi.

November 9.—Urine, 44 oz.; sugar, 3.6 % = 3 xii.

His blood examination showed hæmoglobin 76%, red blood cells 3,360,000, colour index 1.1,

November 10.—Urine, 57 oz.; sugar, 4.2% = 3 xix.; weight, 157 lbs.

November 17.—Urine, 53 oz.; sugar, 4.8% = 3 xx.; weight, 155 lbs.

Ferri et potass. tart., 0.3; *Glyc.*, 1.0; *Liq. arsenicalis*, 0.3; *Aq. ad.*, 8.0; *quater in die.*

November 24.—Urine, 54 oz.; sugar 3.6% = 3 xv.

Liq. arsenicalis, 0.4; *Tr. calumb.*, 1.0; *Glyc.*, 1.0; *Aq. ad*, 4.0; *ter in die*, and *Tab. ferrug.* (Blaud), 0.324; ii., *bis in die.*

On the morning of November 26 a pain came in his epigastrium, and persisted all day, got very bad through the night, and was worse when he called on me on the 27th. He had no nausea or vomiting. He could eat his meals as usual, and had had no purging and no griping pain. The pulse-rate was 96. The temperature in his mouth was normal. The urine contained sugar and a trace of acetone, and no albumin. He was very tender over the liver in the epigastrium and just below it. No friction rub was audible there. He was given *Sod. bicarb.*, 1.0; *Liq. morph. hydrochl.*, 1.0; *Syr. arom.*, 2.0; *Aq. ad.* 15.0 *om. hora*. I was called to see him at 10 p.m. The pain had grown worse through the day, and was agonizing. Pressing in the epigastrium gave exquisite pain. He had *morph. hydrochl.*, 0.016, subcutaneously. He soon dropped off to sleep, and with one or two wakings was quiet till 5 a.m., when he was profusely sick. Next morning he was easy, but had marked epigastric tenderness. He lay in bed six days, and gradually increased his food, which gave him no pain; his bowels moved daily and naturally.

December 4.—He called on me. His weight had fallen to 145 pounds, though he was eating well. Urine, 60 oz.; sugar, 6.8% = 332½. There was no tenderness over the liver or spleen, but some slightly to the left of the mid-line, just above the navel, possibly over the stomach or the pancreas.

December 11.—He had moved about all the week, but had not regained his former endurance, and felt tired behind the knees. He was free from epigastric pain. Urine 114 oz., sugar 7.2% = 3 65½; weight 142½ pounds. His tongue was very red with prominent papillæ and rather sore, and on waking at night "as dry as a chip." His appetite was fair. He was given *Pil. saponis co.* 0.065 *ter in die*. On the night of the 12th he began to vomit, and was sick until seen the next morning, when his pills were stopped and he was given *sod. bicarb.* 1.0, *acidi hydrocyan. dil* 0.26 every two hours. His vomiting ceased at once, and next day he felt well and very hungry.

December 18.—He weighed 134½ pounds, and felt quite strong. Urine 102 oz., sugar 8.4% = 368½. He was given *potass. cit.* 1.2, *glyc.* 1.0, *aq. cinnam.* ad 8.0 *ter in die.*

He was taken to the races on the 23rd, and on the 24th felt tired out and lay about all day. On that night he was sick three times, and once on the morning of the 25th. I saw him at 6 p.m. His pulse was 80 and regular. He felt all right, but any food, even milk and soda water, was not retained. To take *sod. bicarb.* 1.2, *tr. gent. co.* 0.5, *aq. chlorof. ad.* 15.0 4 *quartis horis.*

On the 26th at 9 a.m. his pulse was 140 and weak; he was wandering slightly, had no pain, was not sick, though he had vomited during the night. His medicine was ordered to be given every two hours, and *bism. carb.* 0.75 every hour, if sick. At 5 p.m. his pulse was 180 at the heart, 160 at the wrist. He was quite unconscious, with no râles in the chest. His bowels had not moved, rather a large amount of urine had been passed, 1025, acid, sugar 3.8%, a quite definite cloud of albumin, very marked reaction for acetone, and distinct but not marked for diacetic acid.

On the 27th at 9 a.m. the pulse was 104-108 regular and soft, respirations 36 regular, no râles. The temperature was 101.4° in the axilla. He had been quite comatose all night. His pupils were equal, and of medium size, and reacted slightly to light. His bowels had not moved. No urine was passed. He died quietly about three hours later.

I tried three times to start dieting him for glycosuria, but without benefit; in fact, the first two gastric attacks seemed due to these endeavours.

Several points of interest present themselves in this case. The diagnosis had been given as Addison's disease, and was supported by the marked melasma, and the cardiac

asthenia indicated by his faint or giddy turns of about two years duration and his severe attack in December, 1915, and his subsequent turns of cardiac distress. But the contra-diagnostic was enlargement with induration of the liver, and to a less, though quite definite, degree of the spleen. Not found in *Morbus Addisonii*, this suggested Osler's cirrhosis of hæmochromatosis. But this complaint is attended with glycosuria, and is then identical with bronzed diabetes, the essential signs of which are melasma and glycosuria. When the patient came under my care he had no trace of sugar in the urine, which might have been regarded as overthrowing a diagnosis of bronzed diabetes or Osler's cirrhosis. But, according to him, glycosuria is not an essential or constant concomitant. Melasma and cirrhosis may alone occur, without glycosuria, at least for a long time, and a patient with this disease may die, especially of intercurrent complaint such as enteric fever, without having ever passed pathological sugar in his urine. In the natural history of the affection glycosuria is a late sign, generally a terminal sign, indicating an advanced pathological condition, and followed in less than a year by a fatal termination.

Recognizing the probability, amounting to a certainty, of a gradual reduction of sugar tolerance in such patients, and that mine might be in the transition state when he could perhaps deal with an ordinary but not with an extraordinary carbohydrate diet, I experimented with him by inducing him to take as much sugar and farinaceous food as he could manage for two days, but no sugar reaction was obtained in his urine. His sugar tolerance then must have been fair, and yet forty days afterwards, with an ordinary diet, sugar was voided, and increased so steadily, but rapidly, that in little more than another forty days it had risen from a daily output of 6 or 7 drachms to 65½ and 68½, while his body-weight ran down in the same time from 159 pounds to 134, more than half a pound a day. It was very interesting to catch the case just before the onset of glycosuria, and to watch its fearfully rapid progress.

The blood picture was also of interest. The laboratory expert unacquainted with the nature or history of the case recognized a resemblance to a primary, rather than a secondary, anæmia. At first the question consequently arose: Could this be simply pernicious anæmia with a bronzed skin, which sometimes occurs in this complaint? This suggestion was rebutted by the following considerations: Melasma in pernicious anæmia is quite unusual, is only a mild discolouration, more like "sunburn," and is generally late in onset, being possibly due often to arsenic long and freely taken; besides, hepatic and splenic enlargement do not arise.

A blood picture of a primary anæmia corresponds with the affirmed pathology of the complaint. The primary fault is in the blood, a sort of hæmolysis; hæmoglobin from destroyed corpuscles is deposited in the liver, and excites a chronic interstitial hepatitis, causing cirrhotic enlargement, then in the spleen with chronic splenitis, and lastly in the pancreas with chronic interstitial pancreatitis, destruction of the islands of Langerhans and so glycosuria. One would expect, therefore, a blood picture of primary, rather than of secondary, anæmia, if the suggested pathology is correct.

Another point may be noted—the very early appearance of melasma. This is due to deposit of melanin in the skin consequent on the hæmolysis, which is also laid down in the viscera and tissues, and probably the internal melanosis proceeds simultaneously with the external melasma. From this patient we learn how very early in the complaint such deposit occurs. Two and a half years before he died it attracted the attention of his wife, eighteen months before he himself suspected any disease. It is true he had symptoms, such as drowsiness when sitting at his desk, and occasional slight syncopal or vertiginous turns, of which he thought but lightly, but which were the index of a primary anæmia present and quite definite even then. We may assume a hæmolysis existed for a considerable period before the melasma was sufficiently pronounced to arrest the attention of the laity, and hence it must have had its inception 3 years before he died, and two years before he came under medical observation

Why was it not Banti's disease, in which are found enlarged liver and spleen, anæmia and melasma? Because in this affection (1) splenomegaly is the first sign, and remains throughout the predominant one, the spleen is very large; (2) the anæmia distinctly follows this, and is of a definitely secondary type with leucopenia, and may be periodically intensified by free hæmorrhages, but may also be absent or very slight for years after the splenomegaly has been marked; (3) the hepatic cirrhosis is insignificant compared with the splenomegaly (the reverse of what obtains in Osler's cirrhosis), arises as a terminal condition, generally as a contracted organ, and only occasionally is slightly enlarged; and (4) the melasma is more frequently absent than present, and is seldom so marked as to suggest Addison's disease.

This is the first case which has come under my notice in forty years. Its rarity, as well as its many striking features, must be my excuse for so extended a description and discussion of it.

Reviews.

THE ORIGIN OF TUMOURS.

Theories concerning the origin and essence of neoplasms which are the outcome of serious thought, sound observation and ingenious speculation are not common. The other variety is all too plentiful. C. Mansell Moullin has given us something to think about when he published his short book supplementing his Bradshaw Lecture of 1912 on the biology of tumours.[1] His aim is to place the origin and classification of tumours on a scientific basis. Who can tell whether he has succeeded or not? The critic may accept his arguments, or may deny that they correspond to fact. The author's theories have as much claim to acceptance as the critic's criticisms. Both are matters of opinion. The author's views, however, are as fascinating as they are heterodox, but there is nothing contained in them which is manifestly improbable and nothing that is not in accord with logic. In his preface, Moullin writes when dealing with the possibility of his view being correct:— Time will tell. Perhaps.

He refuses to regard tumours as being either benign or malignant, and comes to a full stop when attempting to classify them according to the tissue from which they are derived. He points out that all cells possess the qualities and capabilities of the cells from which they were derived. No function can be completely lost during the process of evolution. In a remote period primitive organisms reproduced themselves directly or asexually. In multicellular organisms of a higher type certain cells are marked off from the rest and act as germ cells, while the rest are known as the somatic cells. Briefly and imperfectly stated, Mansell Moullin's conception is that one class of tumours arises by the reproduction of germ cells by asexual multiplication, and of somatic cells by means of that reproductive quality which causes the development of parts of an animal or a complete individual to grow from detached segments. He suggests that complicated chemical processes keep normal cells to their normal functions, but when these chemical processes are disturbed, a very small impulse is needed to revive the latent characters of this form of unicellular reproduction. We cannot enter upon the data and observations on which he bases his views in this place. The second class includes tumours which are due to the structural details not being perfectly carried out. Those who take an interest in the problems of descent and of the acquisition of new characters as well as of the inheritance of old ones will find readable material in this short volume.

Dr. L. M. McKillop, of Blackall, Queensland, informs us that he has disposed of his practice to Dr. P. R. Loubet Dr. McKillop has occupied the position of Officer Commanding No. 13 Australian General Hospital at Enoggera with the rank of major. At the termination of his military appointment he proposes to start practice in Brisbane.

[1] The Biology of Tumours, by C. Mansell Moullin, M.A., M.D., F.R.C.S., 1916. H. K. Lewis and Co., Ltd. Demy 8vo., pp. 55. Price, 2s. 6d.